

What is claimed is:

5413
B

1. ~~An oligonucleotide having a nucleotide sequence of from about 13 to about 35 nucleotides that inhibits one or more specific histone deacetylase isoforms, but less than all histone deacetylase isoforms, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA that encodes a portion of one or more histone deacetylase isoforms selected from the group consisting of:~~

- (a) a nucleic acid molecule encoding a portion of HDAC-1 (SEQ ID NO:2),
- (b) a nucleic acid molecule encoding a portion of HDAC-2 (SEQ ID NO:4),
- (c) a nucleic acid molecule encoding a portion of HDAC-3 (SEQ ID NO:6),
- (d) a nucleic acid molecule encoding a portion of HDAC-4 (SEQ ID NO:8),
- (e) a nucleic acid molecule encoding a portion of HDAC-5 (SEQ ID NO:10),
- (f) a nucleic acid molecule encoding a portion of HDAC-6 (SEQ ID NO:12),
- (g) a nucleic acid molecule encoding a portion of HDAC-7 (SEQ ID NO:14), and
- (h) a nucleic acid molecule encoding a portion of HDAC-8 (SEQ ID NO:16).

2. The oligonucleotide according to claim 1, wherein the oligonucleotide is a chimeric oligonucleotide.

3. The oligonucleotide according to claim 1, wherein the oligonucleotide is a hybrid oligonucleotide.

4. The oligonucleotide according to claim 1 having a nucleotide sequence of from about 15 to about 26 nucleotides.

5. The oligonucleotide according to claim 1 having one or more phosphorothioate internucleoside linkage, being 20-26 nucleotides in length, and being modified such that the terminal four nucleotides at the 5' end of the oligonucleotide and the terminal four nucleotides at the 3' end of the oligonucleotide each have 2' -O- methyl groups attached to their sugar residues.

6. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-1 (SEQ ID NO:2).

7. The oligonucleotide according to claim 6 that is SEQ ID NO:17 or SEQ ID No:18.

8. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-2 (SEQ ID NO:4).

9. The oligonucleotide according to claim 8 that is SEQ ID NO:20.

10. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of

HDAC-3 (SEQ ID NO:6).

11. The oligonucleotide according to claim 10 that is SEQ ID NO:22.

12. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-4 (SEQ ID NO:8).

13. The oligonucleotide according to claim 12 that is SEQ ID NO:24 or SEQ ID NO:26.

14. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-5 (SEQ ID NO:10).

15. The oligonucleotide according to claim 14 that is SEQ ID NO:28.

16. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-6 (SEQ ID NO:12).

17. The oligonucleotide according to claim 16 that is SEQ ID NO:29.

18. The oligonucleotide according to claim 6, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-7 (SEQ ID NO:14).

19. The oligonucleotide according to claim 18 that is SEQ ID NO:31.

20. The oligonucleotide according to claim 1, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA encoding a portion of HDAC-8 (SEQ ID NO:16).

21. The oligonucleotide according to claim 20 that is SEQ ID NO:32 or SEQ ID NO:33.

22. A method for inhibiting one or more histone deacetylase isoforms in a cell comprising contacting the cell with the oligonucleotide according to claim 1.

23. The method according to claim 22, wherein cell proliferation is inhibited in the contacted cell.

24. The method according to claim 22, wherein the oligonucleotide that inhibits cell proliferation in a contacted cell induces the contacted cell to undergo growth retardation.

25. The method according to claim 22, wherein the oligonucleotide that inhibits cell proliferation in a contacted cell induces the contacted cell to undergo growth arrest.

26. The method according to claim 22, wherein the oligonucleotide that inhibits cell proliferation in a contacted cell induces the contacted cell to undergo programmed cell death.

27. The method according to claim 22, wherein the oligonucleotide that inhibits cell proliferation in a contacted cell induces the contacted cell to undergo necrotic cell death.

28. A method for inhibiting neoplastic cell proliferation in an animal comprising administering to an animal having at least one neoplastic cell present in its body a therapeutically effective amount of the oligonucleotide of claim 1.

29. The method according to claim 28, wherein the animal is a human.

30. A method for identifying a histone deacetylase isoform that is required for the induction of cell proliferation, the method comprising contacting the histone deacetylase isoform with an oligonucleotide of claim 1, wherein a decrease in the induction of cell proliferation indicates that the histone deacetylase isoform is required for the induction of cell proliferation.

31. A method for identifying a histone deacetylase isoform that is required for cell proliferation, the method comprising contacting the histone deacetylase isoform with an an oligonucleotide of claim 1, wherein a decrease in cell proliferation indicates that the histone deacetylase isoform is required for cell proliferation.

32. A method for identifying a histone deacetylase isoform that is required for the induction of cell differentiation, the method comprising contacting the histone deacetylase isoform with an oligonucleotide of claim 1, wherein an induction of cell differentiation indicates that the histone deacetylase isoform is required for the induction of cell proliferation.

33. A method for modulating cell proliferation comprising contacting a cell with an oligonucleotide of claim 1.

34. The method according to claim 45, wherein the cell proliferation is neoplasia.

35. The method according to claim 46, wherein the histone deacetylase isoform is selected from HDAC-1, HDAC-2, HDAC-3, HDAC-4, HDAC-5, HDAC-6, HDAC-7 and HDAC-8.

36. The method according to claim 47, wherein the histone deacetylase isoform is HDAC-1 and/or HDAC-4.